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nucleic acids, site-directed mutagenesis, interruption of cellular function by binding to specific cellular proteins, and interfering with RNA splicing functions.

#### IN THE CLAIMS

Rewrite the following claims (in accordance with the requirements of 37 C.F.R. 1.12(c)(iii), another version of the rewritten claim(s), on one or more pages separate from this amendment and marked up to show all the changes relative to the previous version of that claim(s), is attached):

1. (Amended) A nucleic acid construct comprising:

a cassette comprised of a sequence coding for a sequence of interest flanked by 3' and 5' complementary sequences comprising an inverted tandem repeat and a sequence coding for a primer binding site in a 3' position with respect to the inverted tandem repeat;

a gene encoding a reverse transcriptase/RNase H; and

a second sequence coding for a sequence of interest between the sequence coding for the inverted tandem repeat and the primer binding site.

4. (Amended) The nucleic acid construct of claim 1 wherein the nucleic acids comprising the sequence comprising the inverted tandem form a stem-loop intermediate with the sequence of interest in the loop and the complementary sequences comprising the inverted tandem repeat form the stem, the nucleic acids comprising the inverted tandem repeat being chosen to provide the stem-loop intermediate with different stabilities depending upon the proportion of ss-DNA to be produced by the first and second sequences of interest.

7. (Amended) An mRNA transcript comprised of a sequence of interest flanked by inverted tandem repeats, a primer binding site located 3' to the inverted tandem repeat, and a second sequence of interest.

#### REMARKS

In the Official Action of December 19, 2000, the informal nature of the drawings, the absence of a sequence listing, and certain informalities in the specification, claims, and Abstract were noted. Claims 1-6 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out and claim that which Applicant regards as the invention, and claim 7 was indicated as being allowable over the prior art.

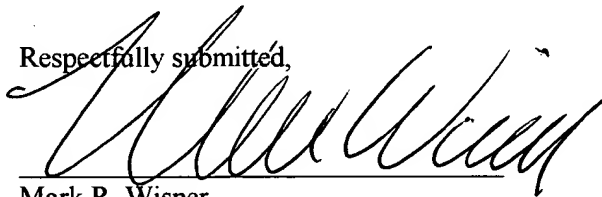
Several replacement paragraphs remedying the informalities noted in the specification and Abstract are set out above. Withdrawal of these objections is respectfully requested in light of these amendments to the specification and Abstract.

It is respectfully requested that the objection to the drawings be held in abeyance until the application is otherwise allowable. 37 C.F.R. 1.85(c), 1.111(b). Responsive to the requirement for a sequence listing, enclosed herewith is a sequence listing complying with the requirements of 37 C.F.R. 1.821 – 1.825, as well as the required Statement to Support Filing and Submission of the sequence listing. Applicant hereby requests that the enclosed sequence listing be entered into the application in place of the sequence listing originally filed with the application.

Responsive to the §112 rejection, Applicant has rewritten claims 1 and 4 as set above. Reconsideration and withdrawal of that rejection is respectfully requested in light of these amendments. Likewise, claim 7 has been amended to correct the informality noted in that claim and withdrawal of the objection to that claim is also requested.

Entry of the above amendments and the enclosed sequence listing, reconsideration and withdrawal of the §112 rejection, allowance of the claims, and passage of the application to issuance are all respectfully requested. In the unforeseen event that there are questions regarding this application, it is respectfully requested that Applicant's counsel be contacted at the address and telephone number set out below.

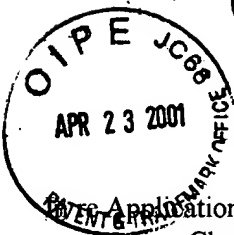
Respectfully submitted,



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ATTORNEY FOR APPLICANT

Date: April 19, 2001



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:  
Charles A. Conrad

Serial No.: 09/397,782

Filed: September 16, 1999

For: **IN VIVO PRODUCTION  
OF ssDNA USING REVERSE  
TRANSCRIPTASE WITH  
PREDEFINED REACTION  
TERMINATION VIA  
STEM-LOOP FORMATION**

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Atty. Docket No.: INGA,004/CIP

Examiner: Martinell

Group Art Unit: 1633

COMMISSIONER OF PATENTS  
AND TRADEMARKS  
WASHINGTON, D.C. 20231

**CERTIFICATE OF MAILING (37 CFR 1.8a)**

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date indicated below with sufficient postage as first class mail in an envelope addressed to the Commissioner of Patent and Trademarks, Washington, D.C. 20231.

Mark R. Wisner, Registration No. 30,603

April 19, 2001

Date

**ATTACHMENT TO RESPONSE TO OFFICIAL  
ACTION OF DECEMBER 19, 2000 (37 C.F.R. 1.121)**

Dear Sir:

In accordance with the requirements of 37 C.F.R. 1.121, Applicant hereby respectfully submits versions of any replacement or added paragraphs, as well as any rewritten claims, on one or more pages separate from the amendment, marked up to show all the changes relative to the previous version of the paragraph(s) and/or claim(s).

**IN THE SPECIFICATION**

The paragraph beginning at page 1, line 6 (referring to the line numbers in the margin of the page) and ending on page 1, line 11 was amended as follows:

This application is a continuation-in-part of my co-pending application Serial No. 09/169,793, entitled PRODUCTION OF ssDNA *IN VIVO*, filed October 9, 1998. Serial No. 09/169,793 is itself a continuation-in-part of application Serial No. 08/877,251, entitled STEM-LOOP CLONING VECTOR AND METHOD, filed June 17, 1997, now issued as Patent No. 6,054,299. Serial No. 08/877,251 is a continuation application of application Serial No. 08/236,504, having the same title, filed April 29, 1994.

The paragraph beginning at page 4, line 30 and ending on page 4, line 32, was amended as follows:

Yet another object of the present invention is to provide a method, and a DNA construct, for producing ssDNA that is [complimentary] complementary to any endogenous nucleic acid sequence target.

#### IN THE ABSTRACT

The Abstract of the Disclosure (page 32 of the specification) was amended as follows:

Methods and compositions for producing single-stranded cDNA (ss-cDNA) with a vector-based system in eukaryotic cells. In one embodiment, the vector comprises plasmid(s) that contain a reverse transcriptase/RNase H gene and a cassette, which includes a sequence coding for a sequence of interest and an inverted repeat, which produces an RNA template from which the reverse transcriptase synthesizes ss-cDNA of a specified sequence. The ss-cDNA [is then modified to remove all flanking vector sequences by taking advantage of the] forms a "stem-loop" structure [of the ss-cDNA, which forms] as a result of the [inclusion of an] inverted tandem repeat [that allows the ss-cDNA to fold back on itself], forming a double stranded DNA stem with the sequence of interest in the loop [portion of this intermediate]. The double-stranded stem may also contain one or more restriction endonuclease recognition sites [and the double-stranded stem of the stem-loop intermediate is] cleaved by the desired corresponding restriction endonuclease(s) so that the loop portion, or sequence of interest, is [then] released as [a linearized,] single-stranded [piece of] DNA. [The plasmid may also include a gene for producing the restriction endonuclease specific for this site in the stem. This released ss-DNA sequence contains minimal sequence information either upstream 5' or downstream 3' from the previous double stranded stem portion which contains the restriction endonuclease cut site.] The plasmid also includes a second sequence of interest 3' to the inverted repeats which is likewise produced with minimal vector sequence.[

]In vivo transfections [using the DNA vector constructs described herein demonstrate the use of this system to produce ss-DNA in eukaryotic cells by taking advantage of the many potential promoter(s)/enhancer(s) signals, polyadenylation signals, splice site junctions, ribosome binding sites, and origin of replication signals known to those skilled in the art. The experiments described

herein] show expression of reverse transcriptase(s)/RNase H(s) within eukaryotic cells as well as synthesis of RNA transcripts which [serve as the template directing the] formation of the ss-cDNA for such therapeutic purposes as gene inactivation using duplex or triplex binding of nucleic acids, site-directed mutagenesis, interruption of cellular function by binding to specific cellular proteins, and interfering with RNA splicing functions.

#### IN THE CLAIMS

Claims 1, 4, and 7 were rewritten as follows:

1. (Amended) A nucleic acid construct comprising:

a cassette comprised of a sequence coding for a sequence of interest flanked by 3' and 5' complementary sequences comprising an inverted tandem [repeats] repeat and [3' distal] a sequence coding for a primer binding site [PBS] in a 3' position with respect to the inverted tandem repeat;

a gene encoding a reverse transcriptase/RNase H; and

a second sequence coding for a sequence of interest between the sequence coding for the inverted tandem [repeats] repeat and the [3' distal] primer binding site [PBS].

4. (Amended) The nucleic acid construct of claim 1 wherein the nucleic acids comprising the sequence comprising the inverted tandem [repeats are designed to form] forms a stem-loop intermediate with the sequence of interest in the loop and the complementary sequences comprising the inverted tandem [repeats forming] repeat form the stem, the [composition of] nucleic acids comprising the inverted tandem repeat being chosen to provide the stem-loop intermediate with different stabilities depending upon the proportion of ss-DNA to be produced by the first and second sequences of interest.

7. (Amended) An mRNA transcript comprised of a sequence of interest flanked by [inverted] inverted tandem repeats, a primer binding site located [3'] 3' to the inverted tandem repeat, and a second sequence of interest.